

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Jannes et al

Atty. Ref.: 2551-59

Divisional of Serial No. 09/448,894

Group:

Filed: August 17, 2001

Examiner:

For: **SIMULTANEOUS DETECTION, IDENTIFICATION AND  
DIFFERENTIATION OF EUBACTERIAL TAXA USING A  
HYBRIDIZATION ASSAY**

\* \* \* \* \*

August 17, 2001

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**PRELIMINARY AMENDMENT**

Preliminarily amend the above-identified application as follows:

**IN THE SPECIFICATION**

Amend the specification as follows:

Page 49, line 1, delete the first paragraph ("FIGURE LEGENDS") and insert the following paragraph therefor:

--BRIEF DESCRIPTION OF THE DRAWINGS--.

Insert the attached Sequence Listing, after the claims pages, and renumber any subsequent pages as required.

## **IN THE ABSTRACT**

Insert the attached Abstract after the claims pages and prior to the Sequence Listing.

## **IN THE CLAIMS**

Amend the claims as follows.

Cancel claims 1-53, without prejudice.

Add the following claims:

--54. (new) A micro-organism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, SEQ ID NO: 169,

SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 195, SEQ ID NO: 196, SEQ ID NO: 197, SEQ ID NO: 213, SEQ ID NO: 214, and SEQ ID NO: 215.

55. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a respiratory tract microorganism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, SEQ ID NO: 169, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129 and SEQ ID NO: 130.

56. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a cerebrospinal fluid microorganism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 116, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 213, SEQ ID NO: 214 and SEQ ID NO: 215.

57. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a uro-genital tract microorganism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of : SEQ ID NO: 122, SEQ ID NO: 123 and SEQ ID NO: 197.

58. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a food sample microorganism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 116, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 213, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 154, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 195 and SEQ ID NO: 196.

59. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a gastrointestinal tract microorganism-specific nucleic acid sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 195 and SEQ ID NO: 196.

60. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium kansasii*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 101, SEQ ID NO: 167, SEQ ID NO: 168 and SEQ ID NO: 169.

61. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium chelonae*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 102, SEQ ID NO: 103 and SEQ ID NO: 174.

62. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium gordonae*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 104, SEQ ID NO: 105 and SEQ ID NO: 106.

63. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium ulcerans* or a *Mycobacterium marinum*-specific sequence comprising the 16S-23S rRNA spacer sequence of SEQ ID NO: 157.

64. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium genavense*-specific sequence comprising a 16S-23S

rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161 and SEQ ID NO: 162.

65. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium simiae*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 164 and SEQ ID NO: 165.

66. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium fortuitum*-specific sequence comprising the 16S-23S rRNA spacer sequence of SEQ ID NO: 166.

67. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium haemophilum*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 171, SEQ ID NO: 172 and SEQ ID NO: 173.

68. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Mycobacterium malmøense*-specific sequence comprising the 16S-23S rRNA spacer sequence of SEQ ID NO: 107.

69. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is *Pseudomonas*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114 and SEQ ID NO: 115.

70. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Staphylococcus aureus*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142 and SEQ ID NO: 143.

71. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Staphylococcus epidermis*-specific sequence comprising the 16S-23S rRNA spacer sequence of SEQ ID NO: 144.

72. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is an *Acinetobacter*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129 and SEQ ID NO: 130.

73. (new) A nucleic acid sequence according to claim 72, wherein said nucleic acid sequence is an *Acinetobacter baumannii*-specific sequence comprising the 16S-23S rRNA spacer sequence of SEQ ID NO: 126.

74. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Listeria*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 116, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 213, SEQ ID NO: 214 and SEQ ID NO: 215.

75. (new) A nucleic acid sequence according to claim 74, wherein said nucleic acid sequence is a *Listeria monocytogenes*-specific sequence comprising the large 16S-23S rRNA spacer sequence of SEQ ID NO: 120.

76. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Brucella*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 131, SEQ ID NO: 132 and SEQ ID NO: 154.

77 (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Salmonella*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137 and SEQ ID NO: 138.



78. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Chlamydia trachomatis*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 123 and SEQ ID NO: 197.

79. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Chlamydia psittaci*-specific sequence comprising the 16S-23S rRNA spacer sequence SEQ ID NO: 122.

80. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Streptococcus*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152 and SEQ ID NO: 153.

81. (new) A nucleic acid sequence according to claim 54, wherein said nucleic acid sequence is a *Yersinia enterocolitica*-specific sequence comprising a 16S-23S rRNA spacer sequence selected from the group consisting of: SEQ ID NO: 195 and SEQ ID NO: 196.

82. (new) Method for the detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) optionally releasing, isolating and/or concentrating the polynucleic acids from a micro-organism to be detected in the sample;
- (ii) optionally amplifying the 16S-23S rRNA spacer region, or a part thereof, from a micro-organism to be detected, with at least one primer pair;
- (iii) detecting the presence of a nucleic acid according to claim 54;
- (iv) identifying the micro-organism present in said sample from the nucleic acid detected in said sample.

83. (new) Method according to claim 82 wherein said detecting comprises sequence analysis of said nucleic acid.

84. (new) A composition comprising a diluent and a sequencing primer that specifically hybridizes with a 16S-23S rRNA spacer sequence of claim 54.

85. (new) A kit for the detection and identification of at least one micro-organism, or for the simultaneous detection and identification of several micro-organisms in a sample comprising a composition according to claim 84.

86. (new) Method according to claim 82 wherein said detecting comprises hybridizing a taxon-specific probe to said nucleic acid, said probe specifically hybridizing with a 16S-23S rRNA spacer sequence of claim 54.

87. (new) A composition comprising a diluent and a taxon-specific probe that specifically hybridizes with a 16S-23S rRNA spacer sequence of claim 54.

88. (new) A kit for the detection and identification of at least one micro-organism, or for the simultaneous detection and identification of several micro-organisms in a sample comprising the following components:

- (i) optionally, at least one primer pair allowing amplification of a 16S-23S rRNA spacer region, or a part thereof;
- (ii) a composition according to claim 87;
- (iii) optionally, a buffer, or components necessary to produce the buffer, enabling a hybridization reaction between a probe of (ii) and a nucleic acid present in a sample, or amplified products thereof;
- (v) optionally, a solution, or components necessary for producing the solution, enabling washing of hybrids formed under the appropriate wash conditions;
- (vi) optionally, a means for detecting the hybrids resulting from hybridization.--

### **REMARKS**

Entry of the above and attached is requested.

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**Divisional of Serial No. 09/448,894**

Claims 1-53 have been canceled, without prejudice. Claims 54-88 have been added and are pending.

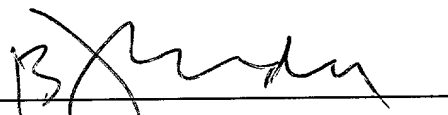
The attached paper copy of the Sequence Listing is the same as that filed in the grand-parent Application No. 08/765,332 and parent Application No. 09/448,894. The Office is requested to use the computer-readable copy of the Sequence Listing from the parent Application No. 09/448,894 and grand-parent Application No. 08/765,332 for the present application. The attached paper copy of the Sequence Listing is the same as the computer-readable copy of the Sequence Listing filed in the parent Application No. 09/448,894 and grand-parent Application No. 08/765,332. No new matter has been added. A separate Request in this regard is attached.

An early and favorable Action on the merits is requested.

Respectfully submitted,

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By: \_\_\_\_\_



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**MARKED UP SPECIFICATION**

Amend the specification as follows:

Page 49, line 1, delete the first paragraph ("FIGURE LEGENDS") and insert the following paragraph therefor:

--BRIEF DESCRIPTION OF THE DRAWINGS--.

**ABSTRACT OF THE DISCLOSURE**

The present invention relates to a method for detection and identification of at least one microorganism, or for the simultaneous detection of several microorganisms in a sample.